

What is claimed is:

- 1 1. A polynucleotide that is regulated by a polypeptide comprising:
2 a regulatable, catalytically active polynucleotide, wherein the peptide interacts with
3 the polynucleotide to affect its catalytic activity.
- 1 2. The polynucleotide of claim 1, wherein the polypeptide is further defined as
2 being a protein.
- 1 3. The polynucleotide of claim 1, wherein the polypeptide comprises a peptide of
2 between about 7 and 20 amino acids.
- 1 4. The polynucleotide of claim 1, wherein the polypeptide comprises a peptide of
2 between about 7 and 12 amino acids.
- 1 5. The polynucleotide of claim 1, wherein the catalytic activity of the nucleic
2 acid is specific for a nucleic acid target sequence.
- 1 6. The polynucleotide of claim 1, wherein the catalytic activity of the nucleic
2 acid is regulated by the interaction of the nucleic acid with an effector.
- 1 7. The polynucleotide of claim 1, wherein the polynucleotide comprises RNA.
- 1 8. The polynucleotide of claim 1, wherein the polynucleotide comprises DNA
- 1 9. The polynucleotide of claim 1, wherein the polynucleotide is at least partially
2 single stranded.
- 1 10. The polynucleotide of claim 1, wherein the polynucleotide is at least partially
2 double stranded.
- 1 11. The polynucleotide of claim 1, wherein the polynucleotide comprises at least
2 one modified base.
- 1 12. The polynucleotide of claim 1, wherein the peptide is endogenous.
- 1 13. The polynucleotide of claim 1, wherein the peptide is exogenous.
- 1 14. The polynucleotide of claim 1, wherein the peptide comprises a
2 phosphorylated peptide.
- 1 15. A nucleic acid that is regulated by an effector comprising:
2 a regulatable, catalytically active nucleic acid, generated by the modification of at
3 least one catalytic residue.

1 16. The nucleic acid of claim 15, wherein the catalytic activity of the nucleic acid
2 is specific for a nucleic acid target sequence.

1 17. The nucleic acid of claim 15, wherein the catalytic activity of the nucleic acid
2 is regulated by the interaction of the nucleic acid with an effector.

1 18. The nucleic acid of claim 15, wherein the nucleic acid comprises RNA.

1 19. The nucleic acid of claim 15, wherein the nucleic acid comprises DNA.

1 20. The nucleic acid of claim 15, wherein the nucleic acid is at least partially
2 single stranded.

1 21. The nucleic acid of claim 15, wherein the nucleic acid is at least partially
2 double stranded.

1 22. The nucleic acid of claim 15, wherein the nucleic acid comprises at least one
2 modified base.

1 23. The nucleic acid of claim 15, wherein the effector is endogenous.

1 24. The nucleic acid of claim 15, wherein the effector is exogenous.

1 25. The nucleic acid of claim 15, wherein the effector comprises a protein.

1 26. The nucleic acid of claim 15, wherein the effector comprises a pharmaceutical
2 agent.

1 27. The nucleic acid of claim 15, wherein the effector comprises a protein
2 complex.

1 28. The nucleic acid of claim 15, wherein the effector comprises a peptide.

1 29. The nucleic acid of claim 15, wherein the effector a phosphorylated peptide.

1 30. The nucleic acid of claim 15, wherein the effector comprises a
2 dephosphorylated peptide.

1 31. The nucleic acid of claim 15, wherein the nucleic acid catalyses a reaction that
2 causes the expression of a target gene to be up-regulated.

1 32. The nucleic acid of claim 15, wherein the nucleic acid catalyses a reaction that
2 causes the expression of a target gene to be down-regulated.

1 33. The nucleic acid of claim 15, wherein the nucleic acid is used to detect at least
2 one exogenous effector from a library of candidate exogenous effector molecules.

1 34. The nucleic acid of claim 15, wherein the nucleic acid and the effector form a
2 nucleic acid-effector complex.

1 35. The nucleic acid of claim 15, wherein the nucleic acid and the effector is a
2 molecule that forms an nucleic acid-effector complex and the nucleic acid-effector complex
3 acts synergistically to affect the catalytic activity of the nucleic acid-effector complex.

1 36. The nucleic acid of claim 15, wherein the nucleic acid catalyses a ligation
2 reaction with an oligonucleotide substrate.

1 37. The nucleic acid of claim 15, wherein the nucleic acid catalyses a reaction that
2 adds a non-oligonucleotide substrate.

1 38. The nucleic acid of claim 15, wherein the nucleic acid catalyses a reaction that
2 adds biotin to the nucleic acid.

1 39. The nucleic acid of claim 15, wherein the nucleic acid catalyses a cleavage
2 reaction with an oligonucleotide substrate.

1 40. The nucleic acid of claim 15, in which the kinetic parameters of nucleic acid
2 catalysis are altered in the presence of one or more effector-effectors that acts on the effector
3 molecule that interacts with the nucleic acid.

1 41. The nucleic acid of claim 15, in which the kinetic parameters of nucleic acid
2 catalysis are altered in the presence of theophylline.

1 42. The nucleic acid of claim 15, in which the kinetic parameters of nucleic acid
2 catalysis are altered in the presence of a supermolecular structure.

1 43. The nucleic acid of claim 15, in which the kinetic parameters of nucleic acid
2 catalysis are altered in the presence of a supermolecular structure that comprises a virus
3 particle.

1 44. The nucleic acid of claim 15, in which the kinetic parameters of nucleic acid
2 catalysis are altered in the presence of a supermolecular structure that comprises a cell wall.

1 45. A nucleic acid comprising:

2 a gene;

3 a regulatable, catalytically active nucleic acid inserted within the gene;

4 wherein the presence of an effector causes the nucleic acid to catalyze a reaction.

1 46. The nucleic acid of claim 45, wherein the catalytic reaction is a self-splicing
2 reaction.

1 47. The nucleic acid of claim 45, wherein the catalytic reaction is a ligation
2 reaction.

1 48. The nucleic acid of claim 45, wherein the catalytic reaction is a trans-cleavage
2 reaction.

1 49. The nucleic acid of claim 45, wherein the catalytic activation of the nucleic
2 acid leads to changes in expression of the gene.

1 50. The nucleic acid of claim 45, wherein the catalytic activation of the nucleic
2 acid leads to changes in expression of one or more genes.

1 51. The nucleic acid of claim 45, wherein the catalytic activation of the nucleic
2 acid leads to changes in expression of the mRNA of the gene.

1 52. The nucleic acid of claim 45, wherein the catalytic activation of the nucleic
2 acid leads to changes in expression of the protein encoded by the gene.

1 53. A nucleic acid segment comprising:
2 a regulatable, catalytically active nucleic acid comprising one or more catalytic
3 nucleotides, selected from a pool of nucleic acids in which at least one of the catalytic
4 residues has been randomized.

1 54. A regulatable, catalytically active nucleic acid segment comprising:
2 an effector domain; and
3 a nucleic acid catalyst domain in which one or more catalytic residues of the nucleic
4 acid catalyst have been randomized;
5 wherein the kinetic parameters of the catalytic domain are regulated by an effector
6 that interacts with the effector domain.

1 55. A method of isolating a regulatable, catalytically active nucleic acid,
2 comprising the steps of:
3 randomizing at least one nucleotide in the catalytic domain of a catalytically active
4 nucleic acid to create a nucleic acid pool; and
5 removing from the nucleic acid pool those nucleic acids that interact with the
6 catalytic target of the catalytic domain.

1 56. The method of claim 55, further comprising the step of adding an effector to
2 the remaining pool of nucleic acids.

1 57. The method of claim 55, further comprising the steps of adding an effector to
2 the remaining nucleic acids, wherein the effector acts on the nucleic acids to alter the
3 catalytic activities of the nucleic acids.

1 58. The method of claim 55, further comprising the step of purifying the isolated
2 nucleic acid.

1 59. The method of claim 55, further comprising the step of sequencing the
2 isolated nucleic acid.

1 60. The method of claim 55, wherein the step of removing the nucleic acids is
2 under high stringency conditions.

1 61. The method of claim 55, wherein the step of removing the nucleic acids is
2 under moderate stringency conditions.

1 62. The method of claim 55, wherein the step of removing the nucleic acids is
2 under low stringency conditions.

1 63. The method of claim 55, where the target is an mRNA molecule.

1 64. The method of claim 56, where the effector is a protein.

1 65. The method of claim 56, where the effector is a peptide.

1 66. The method of claim 56, where the effector is a phosphoprotein.

1 67. The method of claim 56, where the effector is a glycoprotein.

1 68. The method of claim 56, where the effector is light.

1 69. The method of claim 56, where the effector is visible light.

1 70. The method of claim 56, where the effector is a magnet.

1 71. The method of claim 55, where the target is a metabolic reaction.

1 72. The method of claim 55, in which nucleic acids with altered catalytic
2 specificity are selected in the presence of an effector.

1 73. The method of claim 55, in which nucleic acids with altered catalytic
2 activities are selected in the absence of an effector.

1 74. The method of claim 55, in which nucleic acids with altered catalytic
2 activities are serially selected in the presence and the absence of an effector.

1 75. The method of claim 55, the effector domain comprises a random sequence
2 pool.

1 76. The method of claim 55, the effector domain comprises a partially randomized
2 sequence pool.

1 77. A method of making a regulatable, catalytically active nucleic acid,
2 comprising the steps of:

3 contacting a pool of nucleic acids, the nucleic acids having a catalytic and an effector
4 domain, wherein at least one nucleotide in the catalytic domain of the nucleic acids has been
5 randomized;

6 removing from the nucleic acid pool those nucleic acids that interact with the
7 catalytic target of the catalytic domain;

8 adding an effector protein to the remaining nucleic acids; and

9 isolating those nucleic acids that interact with the catalytic target of the catalytic
10 domain.

1 78. A method of isolating a regulatable, catalytically active nucleic acid,
2 comprising the steps of:

3 randomizing at least one nucleotide in the catalytic domain of a catalytically active
4 nucleic acid to create a nucleic acid pool;

5 removing from the nucleic acid pool those nucleic acids that interact with the
6 catalytic target of the catalytic domain;

7 adding an effector molecule to the nucleic acids; and

8 isolating those nucleic acids that interact with the catalytic target of the catalytic
9 domain.

1 79. A method of isolating a regulatable, catalytically active nucleic acid having a
2 catalytic and an effector domain, comprising the steps of:

3 randomizing at least one nucleotide in the catalytic domain of the nucleic acid to
4 create a nucleic acid pool;

5 removing from the nucleic acid pool those randomized nucleic acids that interact with
6 the catalytic target of the catalytic domain;

7 adding an effector to the nucleic acids; and

8 isolating the nucleic acids that interact with the catalytic target of the catalytic
9 domain.

1 80. An automated method of isolating a regulatable, catalytically active nucleic
2 acid having a catalytic and an effector domain, comprising the steps of:

3 (a) randomizing at least one nucleotide in the catalytic domain of the nucleic acid
4 to create a nucleic acid pool;

- 5 (b) removing from the nucleic acid pool those randomized nucleic acids that
6 interact with the catalytic target of the catalytic domain;
7 (c) adding an effector to the nucleic acids;
8 (d) adding an effector-effector that specifically interacts with the effector; and
9 (e) isolating the nucleic acids that interact with the catalytic target of the catalytic
10 domain; and
11 (f) repeating steps (a) through (e).

1 81. A method of detection of a target using a regulatable, catalytically active
2 nucleic acid comprising the steps of:
3 contacting the a regulatable, catalytically active nucleic acid with the target; and
4 measuring the effect of the interaction between the a regulatable, catalytically active
5 nucleic acid and the target.

1 82. A method of modifying a target using a regulatable, catalytically active
2 nucleic acid comprising the steps of:
3 providing a regulatable, catalytically active nucleic acid capable of target specific
4 modification; and
5 modifying the target under conditions that cause a regulatable, catalytically active
6 nucleic acid-specific activity.

1 83. A biosensor comprising:
2 a solid support; and
3 at least one regulatable, catalytically active nucleic acid, wherein the kinetic
4 parameters of the nucleic acid on a target vary in response to the interaction of an effector
5 molecule with the nucleic acid;
6 wherein the at least one regulatable, catalytically active nucleic acid is immobilized
7 on the support.

1 84. The biosensor of claim 83, wherein the reaction is machine readable.

1 85. The biosensor of claim 83, wherein the solid support comprises a multiwell
2 plate.

1 86. The biosensor of claim 83, wherein the solid support comprises a surface
2 plasmon resonance sensor.

1 87. The biosensor of claim 83, wherein the at least one regulatable, catalytically
2 active nucleic acids is covalently immobilized on the solid support.

1 88. The biosensor of claim 83, wherein the catalytic reaction produces a
2 detectable signal.

1 89. The biosensor of claim 83, wherein the catalytic reaction is the attachment of
2 a tag to the immobilized nucleic acids to produce the signal.

1 90. The biosensor of claim 83, wherein the substrate is further defined as
2 containing known nucleic acid sequences tags and the nucleic acids are sorted on the surface
3 of the substrate based on non-covalent hybridization to sequence tags.

1 91. A biosensor comprising:
2 a solid support; and
3 at least one regulatable, catalytically active nucleic acids, wherein the kinetic
4 parameters of the nucleic acids on a target vary in response to the interaction of an effector
5 molecule with the nucleic acid;

6 wherein catalytic targets of the catalytic domain is immobilized on the support.

1 92. A biosensor comprising:
2 a solid support; and
3 at least one regulatable, catalytically active nucleic acids, wherein the kinetic
4 parameters of the nucleic acids on a target vary in response to the interaction of an effector
5 molecule with the nucleic acid;

6 wherein the effector is immobilized on the support.

1 93. A method of selecting a regulatable, catalytically active nucleic acid,
2 comprising the steps of:
3 contacting a pool of nucleic acids, the nucleic acids having a catalytic and an effector
4 domain, wherein at least one nucleotide in the catalytic domain of the nucleic acids has been
5 randomized;

6 removing from the nucleic acid pool those nucleic acids that interact with the
7 catalytic target of the catalytic domain;

8 adding an effector to the remaining nucleic acids; and

9 isolating those nucleic acids that interact with the catalytic target of the catalytic
10 domain;

11 introducing the nucleic acids into a host cell; and
12 measuring the catalytic activity of the nucleic acid upon exposure of the host cell to
13 the effector.

1 94. The method of claim 93, further comprising the step of purifying the isolated
2 nucleic acid.

1 95. The method of claim 93, further comprising the step of sequencing the
2 isolated nucleic acid.

1 96. The method of claim 93, wherein the step of removing the nucleic acids is
2 under high stringency conditions.

1 97. The method of claim 93, wherein the step of removing the nucleic acids is
2 under moderate stringency conditions.

1 98. The method of claim 93, wherein the step of removing the nucleic acids is
2 under low stringency conditions.

1 99. The method of claim 93, where the target is an mRNA molecule.

1 100. The method of claim 93, where the effector is a protein.

1 101. The method of claim 93, where the effector is a peptide.

1 102. The method of claim 93, where the effector is a phosphoprotein.

1 103. The method of claim 93, where the effector is a glycoprotein.

1 104. The method of claim 93, where the effector is light.

1 105. The method of claim 93, where the effector is visible light.

1 106. The method of claim 93, where the effector is a magnet.

1 107. The method of claim 93, in which nucleic acids with altered catalytic
2 activities are serially selected in the presence and the absence of the effector.

1 108. The method of claim 93, the effector domain comprises a completely random
2 sequence pool.

1 109. The method of claim 93, the effector domain comprises a partially randomized
2 sequence pool.

1 110. A method of selecting a regulatable, catalytically active nucleic acid,
2 comprising the steps of:

3 contacting a pool of nucleic acids, the nucleic acids having a catalytic and an effector
4 domain, wherein at least one nucleotide in the catalytic domain of the nucleic acids has been
5 randomized;

6 removing from the nucleic acid pool those nucleic acids that interact with the
7 catalytic target of the catalytic domain;

8 adding an effector to the remaining nucleic acids; and

9 isolating those nucleic acids that interact with the catalytic target of the catalytic
10 domain;

11 introducing the nucleic acids into a host cell; and

12 measuring the catalytic activity of the nucleic acid upon exposure of the host cell to
13 the effector.

1 111. The method of claim 110, further comprising the step of purifying the isolated
2 nucleic acid.

1 112. The method of claim 110, further comprising the step of sequencing the
2 isolated nucleic acid.

1 113. The method of claim 110, wherein the step of removing the nucleic acids is
2 under high stringency conditions.

1 114. The method of claim 110, wherein the step of removing the nucleic acids is
2 under moderate stringency conditions.

1 115. The method of claim 110, wherein the step of removing the nucleic acids is
2 under low stringency conditions.

1 116. The method of claim 110, where the target is an mRNA molecule.

1 117. The method of claim 110, where the effector is a protein.

1 118. The method of claim 110, where the effector is a peptide.

1 119. The method of claim 110, where the effector is a phosphoprotein.

1 120. The method of claim 110, where the effector is a glycoprotein.

1 121. The method of claim 110, where the effector is light.

1 122. The method of claim 110, where the effector is visible light.

1 123. The method of claim 110, where the effector is a magnet.

1 124. The method of claim 110, in which nucleic acids with altered catalytic
2 activities are serially selected in the presence and the absence of the effector.

1 125. The method of claim 110, the effector domain comprises a completely random
2 sequence pool.

1 126. The method of claim 110, the effector domain comprises a partially
2 randomized nucleotide sequence.

1 127. A method of detecting a regulatable, catalytically active nucleic acid,
2 comprising the steps of:

3 isolating a regulatable, catalytically active nucleic acid;

4 creating a construct in which the nucleic acid is in position to regulate the expression
5 of a reporter gene;

6 introducing the construct into a host cell; and

7 measuring the catalytic activity of the nucleic acid upon exposure of the host cell to
8 an effector.

1 128. A vector comprising:

2 a regulatable, catalytically active polynucleotide, wherein the peptide molecule
3 interacts with the polynucleotide to affect its catalytic activity.

1 129. A vector comprising:

2 a regulatable, catalytically active nucleic acid, generated by the modification of at
3 least one catalytic residue.

1 130. A method of modulating expression of a nucleic acid, the method comprising

2 providing a polynucleotide that is regulated by a peptide, the polynucleotide

3 comprising a regulatable, catalytically active polynucleotide, wherein the peptide interacts
4 with the polynucleotide to affect its catalytic activity; and

5 contacting the polynucleotide with the peptide, thereby modulating expression of a
6 nucleic acid.

1 131. The method of claim 130, wherein the polynucleotide is provided in a cell.

1 132. The method of claim 131, wherein the cell is provided in vitro.

1 133. The method of claim 131, wherein the cell is provided in vivo.

1 134. The method of claim 131, wherein the cell is a prokaryotic cell.

1 135. The method of claim 131, wherein the cell is a eukaryotic cell.

1 136. A method of modulating expression of a nucleic acid, the method comprising
2 the steps of:

- 3 providing a nucleic acid that is regulated by an effector, the nucleic acid comprising:
4 a regulatable, catalytically active nucleic acid, wherein the regulatable, catalytically active
5 nucleic acid molecule includes at least one modified catalytic residue; and
6 contacting the nucleic acid with the effector, thereby modulating expression of a
7 nucleic acid.